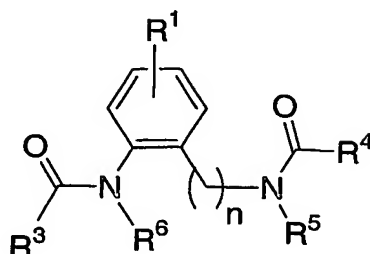


WHAT IS CLAIMED IS:

1. A compound of the formula I:



I

wherein:

R¹ is selected from the group consisting of:

- (1) hydrogen,
- (2) halogen,
- (3) C₁-6alkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl,
- (4) -OC₁-6alkyl,
- (5) -S(O)_m-C₁-6alkyl, wherein m is selected from 0, 1 and 2,
- (6) -CO₂R⁹, wherein R⁹ is independently selected from:
 - (a) hydrogen,
 - (b) -C₁-6alkyl, which is unsubstituted or substituted with 1-6 fluoro,
 - (c) benzyl, and
 - (d) phenyl,
- (7) -NR¹⁰R¹¹, wherein R¹⁰ and R¹¹ are independently selected from:
 - (a) hydrogen,
 - (b) -C₁-6alkyl, which is unsubstituted or substituted with 1-6 fluoro,
 - (c) -C₅-6cycloalkyl,
 - (d) benzyl,
 - (e) phenyl,
 - (f) -S(O)₂-C₁-6alkyl,
 - (g) -S(O)₂-benzyl, and

- (h) -S(O)₂-phenyl,
 (8) -S(O)₂-NR¹⁰R¹¹,
 (9) phenyl, which is unsubstituted or substituted with one or more
 substituents independently selected from:
 5 (a) -C₁₋₆alkyl,
 (b) -O-C₁₋₆alkyl,
 (c) halo,
 (d) hydroxy,
 (e) trifluoromethyl, and
 10 (f) -OCF₃;

R³ is selected from the group consisting of:

- (1) C₁₋₆alkyl, which is unsubstituted or substituted with halogen, hydroxyl
 or phenyl,
 15 (2) C₃₋₇cycloalkyl, which is unsubstituted or substituted with halogen,
 hydroxyl or phenyl, and
 (3) phenyl, which is unsubstituted or substituted with one or more
 substituents independently selected from:
 20 (a) -C₁₋₆alkyl, which is unsubstituted or substituted with
 -NR¹⁰R¹¹,
 (b) -O-C₁₋₆alkyl,
 (c) halo,
 (d) hydroxy,
 (e) trifluoromethyl,
 25 (f) -OCF₃;
 (g) -CO₂R⁹,
 (h) -NR¹⁰R¹¹,
 (i) -C(O)NR¹⁰R¹¹, and
 (j) -NO₂,
 30 (4) heterocycle, wherein heterocycle is selected from:
 benzoimidazolyl, benzimidazolonyl, benzofuranyl, benzofurazanyl,
 benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl,
 carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl,
 indolyl, indolaziny, indazolyl, isobenzofuranyl, isoindolyl,

- 5 isoquinolyl, isothiazolyl, isoxazolyl, naphthpyridinyl, oxadiazolyl, oxazolyl, oxazoline, isoxazoline, oxetanyl, pyranyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazoliny, quinolyl, quinoxaliny, tetrahydropyranyl,
- 10 tetrazolyl, tetrazolopyridyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidiny, 1,4-dioxanyl, hexahydroazepiny, piperazinyl, piperidiny, pyridin-2-onyl, pyrrolidiny, morpholiny, thiomorpholiny, dihydrobenzoimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl,
- 15 dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinoliny, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidiny,
- methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl, and N-oxides thereof, which is unsubstituted or substituted with one or more substituents independently selected from:
- 20 (a) -C₁₋₆alkyl,
- (b) -O-C₁₋₆alkyl,
- (c) halo,
- (d) hydroxy,
- (e) phenyl,
- 25 (f) trifluoromethyl,
- (g) -OCF₃;
- (h) -CO₂R⁹,
- (i) -NR¹⁰R¹¹, and
- (j) -CONR¹⁰R¹¹;
- 30 R⁴ is selected from the group consisting of:
- (1) C₁₋₆alkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl,
- (2) C₃₋₇cycloalkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl, and

- (3) phenyl, which is unsubstituted or substituted with one or more substituents independently selected from:
- (a) -C₁₋₆alkyl,
 - (b) -O-C₁₋₆alkyl,
 - (c) halo,
 - (d) hydroxy,
 - (e) trifluoromethyl,
 - (f) -OCF₃,
 - (g) -CO₂R⁹,
 - (h) -NR¹⁰R¹¹,
 - (i) -CONR¹⁰R¹¹, and
 - (j) -NO₂;
- (4) heterocycle, wherein heterocycle is selected from:
- benzoimidazolyl, benzimidazolonyl, benzofuranyl, benzofurazanyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolaziny, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthpyridinyl, oxadiazolyl, oxazolyl, oxazoline, isoxazoline, oxetanyl, pyranyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, tetrahydropyranyl, tetrazolyl, tetrazolopyridyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidiny, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyridin-2-onyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzoimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidiny, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl, and N-oxides thereof, which is unsubstituted or substituted with one or more substituents independently selected from:

- 5
- (a) -C₁₋₆alkyl,
(b) -O-C₁₋₆alkyl,
(c) halo,
(d) hydroxy,
(e) phenyl,
(f) trifluoromethyl,
(g) -OCF₃,
(h) -CO₂R⁹,
(i) -NR¹⁰R¹¹, and
10 (j) -CONR¹⁰R¹¹;

or wherein R⁴ and R⁵ are joined together to form a phthalimidyl, succinimidyl or glutamidyl ring, which is unsubstituted or substituted with one or more substituents independently selected from the definitions of R¹;

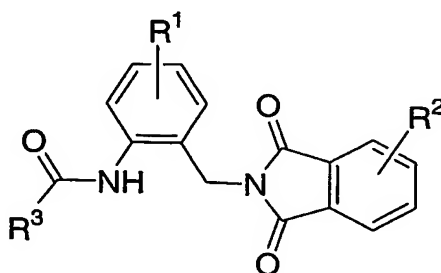
15 R⁵ and R⁶ are independently selected from the group consisting of:

- (1) hydrogen, and
(2) C₁₋₆alkyl;

n is an integer selected from 1, 2 and 3;

20 and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

2. The compound of Claim 1 of the formula Ia:



Ia

25 wherein

R² is selected from the group consisting of:

- (1) hydrogen,
(2) -C₁₋₆alkyl,

(3) -O-C₁₋₆alkyl,

(4) halo,

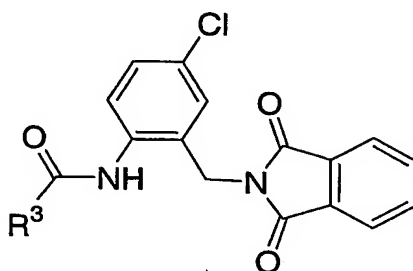
(5) hydroxy,

(6) -NO₂, and

5 (7) phenyl;

and pharmaceutically acceptable salts thereof and individual enantiomers and diastereomers thereof.

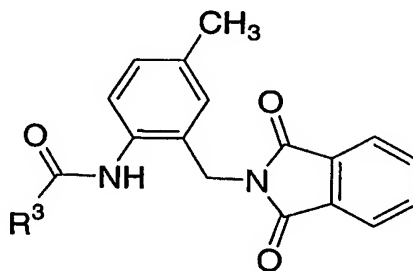
3. The compound of Claim 1 of the formula Ib:



Ib

and pharmaceutically acceptable salts thereof and individual enantiomers and diastereomers thereof.

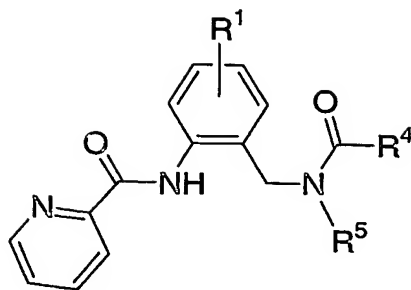
15 4. The compound of Claim 1 of the formula Ic:



Ic

and pharmaceutically acceptable salts thereof and individual enantiomers and diastereomers thereof.

5. The compound of Claim 1 of the formula Id:

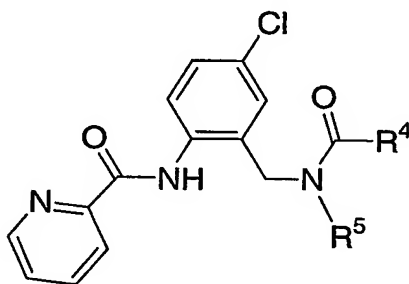


Id

and pharmaceutically acceptable salts thereof and individual enantiomers and diastereomers thereof.

5

6. The compound of Claim 1 of the formula Ie:

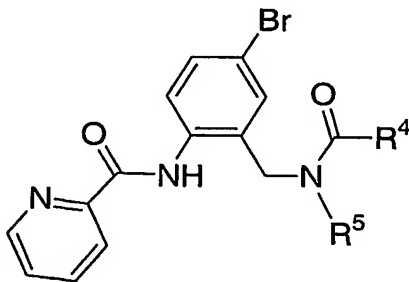


Ie

and pharmaceutically acceptable salts thereof and individual enantiomers and diastereomers thereof.

10

7. The compound of Claim 1 of the formula If:



If

and pharmaceutically acceptable salts thereof and individual enantiomers and diastereomers thereof.

- 5 8. The compound of Claim 1 wherein R^1 is hydrogen.
9. The compound of Claim 1 wherein R^2 is halogen.
10. The compound of Claim 1 wherein R^2 is fluoro.
- 10 11. The compound of Claim 1 wherein R^2 is chloro.
12. The compound of Claim 1 wherein R^2 is bromo.
13. The compound of Claim 1 wherein R^2 is methyl.
- 15 14. The compound of Claim 1 wherein R^3 is phenyl, which is
unsubstituted or substituted with one or more substituents independently selected
from:
- 20 (a) -C₁₋₆alkyl,
 (b) -O-C₁₋₆alkyl,
 (c) halo,
 (d) hydroxy,
 (e) trifluoromethyl,
 (f) -OCF₃;
25 (g) -CO₂-C₁₋₆alkyl,
 (h) -NH₂,
 (i) -NH-C₁₋₆alkyl,
 (j) -CONH₂, and
 (k) -CONH-C₁₋₆alkyl.
- 30 15. The compound of Claim 1 wherein R^3 is phenyl, which is
unsubstituted or substituted with hydroxy, halo, -CONHC₁₋₆alkyl or -CO₂C₁₋₆alkyl.
- 35 16. The compound of Claim 1 wherein R^3 is pyridyl, pyrimidinyl,
pyrazinyl, pyridazinyl, piperazinyl, furanyl or thienyl.

17. The compound of Claim 1 wherein R⁴ and R⁵ are joined together to form a phthalimidyl ring.
- 5 18. The compound of Claim 1 wherein R⁵ is hydrogen or C₁₋₆alkyl.
19. The compound of Claim 1 wherein R⁶ is hydrogen.
- 10 20. The compound of Claim 1 wherein n is 1.
21. A compound which is selected from the group consisting of:
- N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-2-hydroxybenzamide;
- 15 N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyrimidine-2-carboxamide;
- 20 N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-2-hydroxybenzamide;
- 2-[(2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl)amino]carbonyl]phenyl;
- N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl}-2-hydroxybenzamide;
- 25 2-chloro-N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl}benzamide;
- N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl}-2-fluorobenzamide;
- N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl}benzamide;
- 30 N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl}-3,5-difluorobenzamide;
- N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;

- N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-3-methoxybenzamide;
- N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-2-methylbenzamide;
- 5 N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-2-furamide;
- N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-5-methylisoxazole-3-carboxamide;
- 10 N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}cyclohexanecarboxamide;
- N-{5-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}cyclohexanecarboxamide;
- N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-1-methyl-1H-imidazole-2-carboxamide;
- 15 N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-1,3-thiazole-4-carboxamide;
- N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-3-hydroxypyridine-2-carboxamide;
- N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}imidazo[2,1-b][1,3]thiazole-6-carboxamide;
- 20 N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-1,2,5-thiadiazole-3-carboxamide;
- N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-4-methoxyphenyl}pyridine-2-carboxamide;
- 25 N-{4-bromo-2-[(4-fluoro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- N-{4-chloro-2-[(2,5-dioxo-3-phenyl-2,5-dihydro-1H-pyrrol-1-yl)methyl]phenyl}pyridine-2-carboxamide;
- N-{4-chloro-2-[(4-fluoro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- 30 N-{4-chloro-2-[(5,6-dimethyl-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- N-{4-chloro-2-[(5-fluoro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;

- N-{4-chloro-2-[(5-ethoxy-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- N-{5-bromo-3-[(5,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]pyridin-2-yl}pyridine-2-carboxamide;
- 5 N-{4-chloro-2-[(5-hydroxy-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- N-{4-bromo-2-[(5-fluoro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- N-{4-bromo-2-[(5-ethoxy-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- 10 N-{4-bromo-2-[(5,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- N-{4-bromo-2-[(4,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- 15 N-{2-[(4,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-4-fluorophenyl}pyridine-2-carboxamide;
- N-{2-[(5,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-4-fluorophenyl}pyridine-2-carboxamide;
- N-{4-fluoro-2-[(5-nitro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
- 20 N-{4-bromo-2-[(4-methyl-1,3-dioxo-3,4,5,6-tetrahydrocyclopenta[c]-pyrrol-2(1H)-yl)methyl]phenyl}pyridine-2-carboxamide;
- N-{5-bromo-2-[(pyridin-2-ylcarbonyl)amino]benzyl}pyridine-2-carboxamide;
- 25 N-(4-bromo-2-[(2-fluorobenzoyl)amino]methyl)phenylpyridine-2-carboxamide;
- N-{5-bromo-2-[(pyridin-2-ylcarbonyl)amino]benzyl}pyridine-2-carboxamide;
- N-[4-bromo-2-([2-(trifluoromethyl)benzoyl]amino)methyl]phenylpyridine-2-carboxamide;
- 30 N-(4-chloro-2-[(3,5-dichlorobenzoyl)(ethyl)amino]methyl)phenylpyridine-2-carboxamide;
- N-(2-[(4-butoxybenzoyl)(ethyl)amino]methyl)-4-chlorophenylpyridine-2-carboxamide;

N-(4-chloro-2-{{(3,5-dimethoxybenzoyl)(ethyl)amino}methyl}phenyl)pyridine-2-carboxamide;
N-(4-chloro-2-{{(3,4-dichlorobenzoyl)(ethyl)amino}methyl}phenyl)pyridine-2-carboxamide;
5 N-(4-chloro-2-{{(3,5-dichlorobenzoyl)(isobutyl)amino}methyl}phenyl)pyridine-2-carboxamide;
N-(4-chloro-2-{{(3,5-dimethoxybenzoyl)(isobutyl)amino}methyl}phenyl)pyridine-2-carboxamide;
N-{5-fluoro-2-[(pyridin-2-ylcarbonyl)amino]benzyl}quinoxaline-2-
10 carboxamide;
N-(2-{{(4-butoxybenzoyl)amino}methyl}-4-fluorophenyl)pyridine-2-carboxamide;
N-(4-bromo-2-{{(3-methoxybenzoyl)(methyl)amino}methyl}phenyl)pyridine-2-carboxamide;
15 N-(4-chloro-2-{{(3,5-dichlorobenzoyl)(methyl)amino}methyl}phenyl)pyridine-2-carboxamide;
N-(2-{{[3,5-bis(trifluoromethyl)benzoyl](methyl)amino}methyl}-4-chlorophenyl)pyridine-2-carboxamide;
N-[4-chloro-2-{{(3,5-dichlorobenzoyl)[2-(dimethylamino)ethyl]amino}methyl}-phenyl]pyridine-2-carboxamide;
20 N-[2-(benzoylamino)-5-bromobenzyl]-N,3,5-trimethylbenzamide;
N-(4-bromo-2-{{(3,5-dichlorobenzoyl)(methyl)amino}methyl}-phenyl)pyridine-2-carboxamide;
N-(4-bromo-2-{{(3,4-difluorobenzoyl)(methyl)amino}methyl}phenyl)-
25 pyridine-2-carboxamide;
N-(4-bromo-2-{{(2,4-difluorobenzoyl)(methyl)amino}methyl}phenyl)-
pyridine-2-carboxamide;
N-(4-bromo-2-{{(3,4-dichlorobenzoyl)(methyl)amino}methyl}phenyl)-
pyridine-2-carboxamide;
30 N-[4-chloro-2-{{methyl[2-(trifluoromethyl)benzoyl]amino}methyl}-phenyl]pyridine-2-carboxamide;
N-(4-chloro-2-{{(3,4-dichlorobenzoyl)(methyl)amino}methyl}-phenyl)pyridine-2-carboxamide;
and pharmaceutically acceptable salts thereof.

35

22. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

5 23. A method for potentiation or inhibition of metabotropic glutamate receptor activity in a mammal which comprises the administration of an effective amount of the compound of Claim 1.

10 24. A method for the manufacture of a medicament for potentiation or inhibition of metabotropic glutamate receptor activity in a mammal comprising combining the compound of Claim 1 with a pharmaceutical carrier or diluent.

15 25. A method for treating, controlling, ameliorating or reducing the risk of a neurological and psychiatric disorders associated with glutamate dysfunction in a mammalian patient in need of such which comprises administering to the patient a therapeutically effective amount of a compound of Claim 1.

20 26. A method for treating, controlling, ameliorating or reducing the risk of schizophrenia in a mammalian patient in need of such which comprises administering to the patient a therapeutically effective amount of a compound of Claim 1.

25 27. A method for treating, controlling, ameliorating or reducing the risk of anxiety in a mammalian patient in need of such which comprises administering to the patient a therapeutically effective amount of a compound of Claim 1.